

CLAIMS

WE CLAIM:

- ✓ 1. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- 5 a) obtaining a nucleic acid sample from the individual; and
- b) determining the nucleotide present at nucleotide position 2210 of the thrombospondin-1 gene,
- wherein presence of a G at nucleotide position 2210 is indicative of increased likelihood of a vascular disease in the individual as compared with an individual
- 10 having an A at nucleotide position 2210.
2. The method of Claim 1, wherein the thrombospondin-1 gene has the nucleotide sequence of SEQ ID NO: 1.
3. The method of Claim 1, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction,
- 15 stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
4. The method of Claim 3, wherein the vascular disease is myocardial infarction.
5. The method of Claim 3, wherein the vascular disease is coronary heart disease.
- ✓ 6. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- 20 a) obtaining a nucleic acid sample from the individual; and

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- b) determining the nucleotide present at nucleotide position 2210 of the thrombospondin-1 gene,
wherein presence of an A at nucleotide position 2210 is indicative of decreased likelihood of a vascular disease in the individual as compared with an individual
5 having a G at nucleotide position 2210.
7. The method according to Claim 6, wherein the thrombospondin-1 gene has the nucleotide sequence of SEQ ID NO: 1.
8. The method according to Claim 6, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial
10 infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
9. The method according to Claim 8, wherein the vascular disease is myocardial infarction.
10. The method according to Claim 8, wherein the vascular disease is coronary heart
15 disease.
- ✓ 11. A method for predicting the likelihood that an individual will have a vascular disease, comprising the steps of:
- a) obtaining a DNA sample from an individual to be assessed; and
b) determining the nucleotide present at nucleotide position 2210 of the
20 thrombospondin-1 gene,
wherein presence of a G at nucleotide position 2210 is indicative of increased likelihood of a vascular disease in the individual as compared with an individual having an A at nucleotide position 2210.

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12. The method according to Claim 11, wherein the thrombospondin-1 gene has the nucleotide sequence of SEQ ID NO: 1.
13. The method according to Claim 11, wherein the individual is an individual at risk for development of a vascular disease.
- 5 14. The method according to Claim 11, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
- 10 15. The method according to Claim 14, wherein the vascular disease is myocardial infarction.
16. The method according to Claim 14, wherein the vascular disease is coronary heart disease.
- 15 17. A nucleic acid molecule comprising all or a portion of the nucleic acid sequence of SEQ ID NO: 1 wherein said nucleic acid molecule is at least 10 nucleotides in length and wherein the nucleic acid sequence comprises a polymorphic site at nucleotide position 2210 of SEQ ID NO: 1.
18. The nucleic acid molecule according to Claim 17, wherein the nucleotide at the polymorphic site is different from a nucleotide at the polymorphic site in a corresponding reference allele.
- 20 19. An allele-specific oligonucleotide that hybridizes to the nucleic acid molecule of Claim 17.

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20. A peptide of SEQ ID NO: 2 which is at least ten contiguous amino acids, wherein the peptide comprises the serine at amino acid position 700 of SEQ ID NO: 2.
21. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- 5 a) obtaining a biological sample comprising thrombospondin-1 protein or relevant portion thereof from the individual; and
- b) determining the amino acid present at amino acid position 700 of the thrombospondin-1 protein,
- 10 wherein presence of an asparagine at amino acid position 700 is indicative of increased likelihood of a vascular disease in the individual as compared with an individual having a serine at amino acid position 700.
22. The method of Claim 21, wherein the thrombospondin-1 protein has the amino acid sequence of SEQ ID NO: 2.
23. The method of Claim 22, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction,
- 15 stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
24. The method of Claim 23, wherein the vascular disease is myocardial infarction.
25. The method of Claim 23, wherein the vascular disease is coronary heart disease.
- 20 26. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- a) obtaining a biological sample comprising thrombospondin-1 protein or relevant portion thereof from the individual; and

- b) determining the amino acid present at amino acid position 700 of the thrombospondin-1 protein,
wherein presence of a serine at amino acid position 700 is indicative of reduced likelihood of a vascular disease in the individual as compared with an individual
5 having an asparagine at amino acid position 700.
27. The method according to Claim 26, wherein the thrombospondin-1 protein has the amino acid sequence of SEQ ID NO: 2.
28. The method according to Claim 26, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial
10 infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
29. The method of Claim 28, wherein the vascular disease is myocardial infarction.
30. The method of Claim 28, wherein the vascular disease is coronary heart disease.
31. A method of diagnosing or aiding in the diagnosis of a vascular disease in an
15 individual comprising
- a) obtaining a nucleic acid sample from the individual; and
- b) determining the nucleotide present at nucleotide position 1186 of the thrombospondin-4 gene,
wherein presence of a C at nucleotide position 1186 is indicative of increased
20 likelihood of a vascular disease in the individual as compared with an individual having an G at nucleotide position 1186.
32. The method of Claim 31, wherein the thrombospondin-4 gene has the nucleotide sequence of SEQ ID NO: 3.

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33. The method of Claim 31, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
- 5 34. The method of Claim 33, wherein the vascular disease is myocardial infarction.
35. The method of Claim 33, wherein the vascular disease is coronary heart disease.
- ✓ 36. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- 10 a) obtaining a nucleic acid sample from the individual; and
- b) determining the nucleotide present at nucleotide position 1186 of the thrombospondin-4 gene,
- wherein presence of a G at nucleotide position 1186 is indicative of decreased likelihood of a vascular disease in the individual as compared with an individual having a C at nucleotide position 1186.
- 15 37. The method according to Claim 36, wherein the thrombospondin-4 gene has the nucleotide sequence of SEQ ID NO: 3.
38. The method according to Claim 36, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and
- 20 pulmonary embolism.
39. The method according to Claim 38, wherein the vascular disease is myocardial infarction.

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40. The method according to Claim 38, wherein the vascular disease is coronary heart disease.
41. A method for predicting the likelihood that an individual will have a vascular disease, comprising the steps of:
- 5 a) obtaining a DNA sample from an individual to be assessed; and
- b) determining the nucleotide present at nucleotide position 1186 of the thrombospondin-4 gene,
- wherein presence of a C at nucleotide position 1186 is indicative of increased likelihood of a vascular disease in the individual as compared with an individual
- 10 having a G at nucleotide position 1186.
42. The method according to Claim 41, wherein the thrombospondin-4 gene has the nucleotide sequence of SEQ ID NO: 3.
43. The method according to Claim 41, wherein the individual is an individual at risk for development of a vascular disease.
- 15 44. The method according to Claim 41, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
45. The method according to Claim 44, wherein the vascular disease is myocardial
- 20 infarction.
46. The method according to Claim 44, wherein the vascular disease is coronary heart disease.

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47. A nucleic acid molecule comprising all or a portion of the nucleic acid sequence of SEQ ID NO: 3 wherein said nucleic acid molecule is at least 10 nucleotides in length and wherein the nucleic acid sequence comprises a polymorphic site at nucleotide position 1186 of SEQ ID NO: 3.
48. The nucleic acid molecule according to Claim 47, wherein the nucleotide at the polymorphic site is different from a nucleotide at the polymorphic site in a corresponding reference allele.
49. An allele-specific oligonucleotide that hybridizes to the nucleic acid molecule of Claim 47.
50. A peptide of SEQ ID NO: 4 which is at least ten contiguous amino acids, wherein the peptide comprises the proline at amino acid position 387 of SEQ ID NO: 4.
51. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- a) obtaining a biological sample comprising thrombospondin-4 protein or relevant portion thereof from the individual; and
- b) determining the amino acid present at amino acid position 387 of the thrombospondin-4 protein,
- wherein presence of an alanine at amino acid position 387 is indicative of increased likelihood of a vascular disease in the individual as compared with an individual having a proline at amino acid position 387.
52. The method of Claim 51, wherein the thrombospondin-4 protein has the amino acid sequence of SEQ ID NO: 4.

53. The method of Claim 52, wherein the vascular disease is selected from the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
- 5 54. The method of Claim 53, wherein the vascular disease is myocardial infarction.
55. The method of Claim 53, wherein the vascular disease is coronary heart disease.
- ✓ 56. A method of diagnosing or aiding in the diagnosis of a vascular disease in an individual comprising
- 10 a) obtaining a biological sample comprising thrombospondin-4 protein or relevant portion thereof from the individual; and
- b) determining the amino acid present at amino acid position 387 of the thrombospondin-4 protein,
- wherein presence of a proline at amino acid position 387 is indicative of reduced likelihood of a vascular disease in the individual as compared with an individual
- 15 having an alanine at amino acid position 387.
57. The method according to Claim 56, wherein the thrombospondin-4 protein has the amino acid sequence of SEQ ID NO: 4.
58. The method according to Claim 56, wherein the vascular disease is selected from
- 20 the group consisting of atherosclerosis, coronary heart disease, myocardial infarction, stroke, peripheral vascular diseases, venous thromboembolism and pulmonary embolism.
59. The method of Claim 58, wherein the vascular disease is myocardial infarction.

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60. The method of Claim 58, wherein the vascular disease is coronary heart disease.
61. A nucleic acid molecule selected from the group consisting of the genes listed in the Table, wherein said nucleic acid molecule is at least 10 nucleotides in length and comprises a polymorphic site identified in the Table, wherein a nucleotide at the polymorphic site is different from a nucleotide at the polymorphic site in a corresponding reference allele.
62. A nucleic acid molecule according to Claim 61, wherein said nucleic acid molecule is at least 15 nucleotides in length.
63. A nucleic acid molecule according to Claim 61, wherein said nucleic acid molecule is at least 20 nucleotides in length.
64. A nucleic acid molecule according to Claim 61, wherein the nucleotide at the polymorphic site is the variant nucleotide for the gene listed in the Table.
65. An allele-specific oligonucleotide that hybridizes to a portion of a gene selected from the group consisting of the genes listed in the Table, wherein said portion is at least 10 nucleotides in length and comprises a polymorphic site identified in the Table, wherein a nucleotide at the polymorphic site is different from a nucleotide at the polymorphic site in a corresponding reference allele.
66. An allele-specific oligonucleotide according to Claim 65 that is a probe.
67. An allele-specific oligonucleotide according to Claim 65, wherein a central position of the probe aligns with the polymorphic site of the portion.
68. An allele-specific oligonucleotide according to Claim 65 that is a primer.

69. An allele-specific oligonucleotide according to Claim 68, wherein the 3' end of the primer aligns with the polymorphic site of the portion.
70. An isolated gene product encoded by a nucleic acid molecule according to Claim 61.
- ✓ 5 71. A method of analyzing a nucleic acid sample, comprising obtaining the nucleic acid sample from an individual; and determining a base occupying any one of the polymorphic sites shown in the Table.
- 10 72. A method according to Claim 71, wherein the nucleic acid sample is obtained from a plurality of individuals, and a base occupying one of the polymorphic positions is determined in each of the individuals, and wherein the method further comprising testing each individual for the presence of a disease phenotype, and correlating the presence of the disease phenotype with the base.

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